COMPLETED PROJECT REPORT

Project Title: A 91−day oral toxicity study in rats with zinc phosphide technical

Research Agency: National Wildlife Research Center

Principal Investigator: J. Siglin

Budget: $105,009

Background:

This study was conducted to satisfy a request by the U. S. Environmental Protection Agency to provide data on the mutagenic potential of zinc phosphide. These data are required to maintain registration of the zinc phosphide baits in California.

Objectives:

This study was performed to determine and evaluate the potential toxicity of zinc phosphide technical when administered orally to rats for a minimum of 91 consecutive days.

Summary:

The study consisted of a control group and three treatment groups, with ten animals per sex in each group. The test substance was mixed with the vehicle (propylene glycol) and administered at dosage levels of 0.1, 1.0, and 3.0 mg/kg/day. All doses were given at a constant volume of 2.0 mL/kg. Control animals were administered the vehicle under the same experimental conditions and at an equivalent dose volume. The rats were observed daily for clinical signs of toxicity, and body weights and food consumption were measured weekly. Blood and urine were obtained from all surviving animals at study termination for evaluation of hematology, clinical biochemistry, and urinalysis parameters. Each rat was subjected to a complete gross necropsy examination. Fresh organ weights were obtained for surviving animals, and selected tissues were preserved from all rats. All tissues from control and high−dose rats, and rats found dead or euthanatized moribund, and the lungs, liver, kidneys, and gross lesions from all low− and mid−dose rats were examined microscopically.

One male rat of the 1.0 mg/kg/day group, and seven rats of the 3.0 mg/kg/day group (two males and five females) died or were euthanatized moribund during the study. In these rats, clinical signs prior to death ranged from no remarkable findings to several abnormal clinical observations. Clinical observations in animals which survived at the 1.0 and 3.0 mg/kg/day levels were generally unremarkable, and there were no apparent test substance−related clinical signs in males or females of the 0.1 mg/kg/day group. There were no toxicologically meaningful differences among the groups with respect to body weights, weight gain, or food consumption. Erthrocyte counts, hemoglobin concentration, and hematocrit were slightly, but statistically

decreased in males which received 1.0 and 3.0 mg/kg/day, and in females given 3.0 mg/kg/day. In males rats, total bilirubin was statistically increased RBC destruction, as indicated by decreased RBC counts in these groups. There were no statistical differences in serum biochemistry parameters in the female rats. Urine pH was decreased slightly in the 1.0 and 3.0 mg/kg/day males and females. No test substance−related ocular lesions were observed in the zinc phosphide technical treated animals. In the female rats, absolute heart weight, and heart weight relative to body and brain weight, were statistically increased at the 3.0 mg/kg/day level. In addition, liver weight relative to body and brain weight was statistically increased in the 3.0 mg/kg/day females. However, these organ weight differences did not correlate with any abnormal clinical biochemistry or histopathological changes in the rats. There were no meaningful differences in organ changes or death mechanisms attributable to test substance treatment. Although several relationship with the test substance was regarded as equivocal. A slightly increased prevalence and severity of splenic hemosiderosis in the 3.0 mg/kg/day females was considered a possible test substance effect.

Based on the results of this study, a dosage level of 0.1 mg/kg/day was considered a no−observed effect level (NOEL) for 91−day oral (gavage) administration of zinc phosphide technical in rats.